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Pisa syndrome after unilateral pallidotomy in Parkinson's disease: an unrecognised, delayed adverse event?

Dystonic lateroflexion of the trunk, also referred to as Pisa syndrome, pleurothotonus or a lean to the side, was originally described in association with prior exposure to neuroleptics. However, axial deformities (Pisa syndrome, camptocormia and antecollis) are also well recognised but poorly understood features of multiple system atrophy or late-stage Parkinson's disease. Here, we report on three patients with longstanding Parkinson's disease who, 4–9 years after a left pallidotomy, developed a Pisa syndrome to the right.

Case histories

The first patient, now 72 years old, was diagnosed with Parkinson's disease at age 44 years, after initially presenting with pain in his right arm and leg. The right side always remained the more affected and the dyskinesias that developed after 4 years of levodopa treatment were also more pronounced on the right side. Because of progressive motor fluctuations, a left-sided pallidotomy was performed after 17 years of disease, which resulted in abolition of the right-sided dyskinesias and an improvement in the tremor and rigidity on the right. Eight years after the pallidotomy, 25 years after disease onset, he gradually developed a lean to the right, which showed some diurnal fluctuation and responded modestly to dopaminergic treatment. When ''on'', he still remains independent for most daily activities. Parkinson's disease dementia has recently been diagnosed.

In the second patient, now 63 years old, Parkinson's disease was diagnosed at the age of 47 years when he first noticed decreased dexterity and a tremor of his right hand. He developed limb dyskinesias (more on the right side than on the left) after only 1 year of levodopa treatment. After unsuccessful alternative drug regimens, a left-sided pallidotomy was performed after 6 years of disease. The dyskinesias on the right completely disappeared and a beneficial effect on tremor and walking were documented. Fifteen years after his first symptoms, and about 9 years after surgery, a lean to the right evolved that was unresponsive to dopaminergic drugs. Over the past year, he has developed features of early Parkinson's disease dementia. He uses a wheelchair for outdoor activities only.

The third patient, now 69 years old, noticed a tremor of his right hand when he was 43 years old. Dyskinesias, mainly on the right, became apparent 3 years after levodopa treatment. Seventeen years after onset, he underwent a left-sided pallidotomy. The dyskinesias on the right side subsided, and he also experienced ''off''-period improvement and better balance. In his 21st year of disease, 4 years after the pallidotomy, he developed a mild torticollis to the right. Around the same time, he started to gradually develop a lean to the right (fig 1), sometimes causing him to fall out of a chair. Mild Parkinson's disease dementia was established recently. He is still able to walk unsupported.

Comment

The outcome and follow-up after a median 14 months of 26 patients with Parkinson's disease who underwent a unilateral medial pallidotomy in our hospital in 1995–96 have been reported previously.[1] Here, we describe the further follow-up of three of these patients, because they developed a marked lean (Pisa syndrome) to the right side 4–9 years after a left pallidotomy, at disease durations of 15–25 years. The truncal lateroflexion came on gradually, and showed some diurnal fluctuation and dopamine responsiveness in only one patient. In all patients, signs and symptoms started and remained more pronounced on the right side, which was also the more dyskinetic side, hence the choice of a left-sided pallidotomy. Despite the long disease duration, mobility was still relatively well preserved, particularly in patients 1 and 3, and the dyskinesias continued to be less severe on the side contralateral to the pallidotomy.

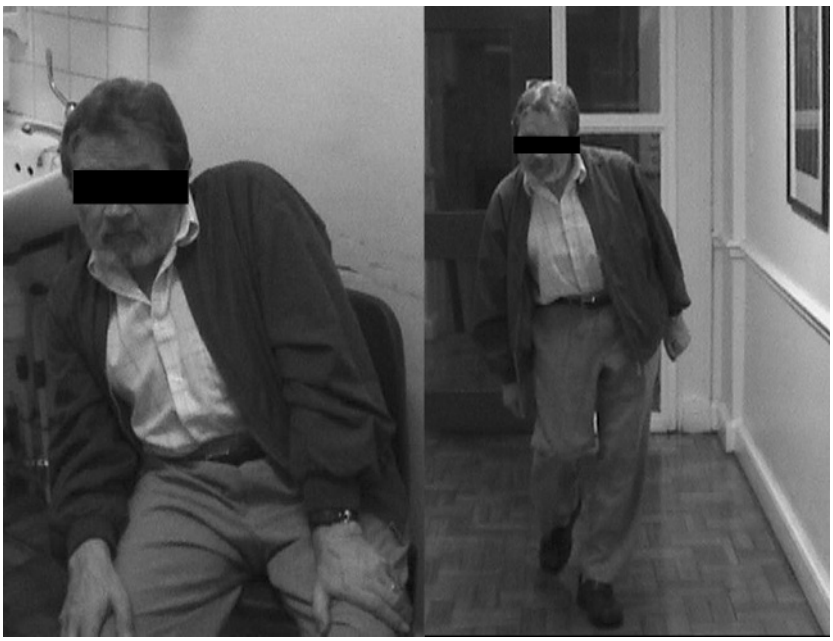

Figure 1 A 69-year-old man with a 26-year history of Parkinson's disease underwent a left pallidotomy 9 years ago. Four years after this procedure, he gradually developed a lean to the right. These photographs show the marked lean to the right, which is present during both sitting and walking, as well as a mild head tilt to the left. Informed consent was obtained for publication of this figure.

Importantly, postoperative imaging in these three patients confirmed that the lesions were confined to the medial pallidum (without extension to the internal capsule or lateral pallidum as observed in four others).[1]

Although we did not perform magnetic resonance imaging or electromyography studies of the paraspinal muscles, we believe that this truncal lateroflexion results from dystonia or asymmetric rigidity and not from a unilateral paraspinal myopathy.

The main question is whether this leaning towards one side is merely a phenomenon of an advanced stage Parkinson's disease or a hitherto unrecognised delayed-onset consequence of unilateral pallidotomy in Parkinson's disease.

Unilateral pallidal lesions in rats result in curling and head turning towards the side contralateral to the lesion.[2] The rarely reported acquired unilateral pallidal lesions in humans seem to particularly give rise to contralateral limb dystonia, hemidystonia or hemiparkinsonism rather than to axial abnormalities.[3] If the leaning in our patients is directly related to the pallidum lesion, the delay of 4–9 years after pallidotomy is rather difficult to explain, although delayed-onset progressive dystonia has been reported in bilateral anoxic pallidal lesions.

Previous observations noted the common presence of scoliosis in Parkinson's disease and postencephalitic parkinsonism, which was usually concave to the clinically less affected side—that is, directed towards the side with more severe nigrostriatal pathology.[4 5] This is corroborated by animal studies, as rodents with unilateral lesions of the substantia nigra display a deviated spinal curvature and/or abnormal turning behaviour directed towards the lesioned side; however, when these animals are given dopaminergic agents, their body asymmetry reverses from ipsiversive to contraversive.[6] In a 6-hydroxydopamine rat model of Parkinson's disease, with a unilateral substantia nigra lesion causing ipsiversive body axis deviation without and contraversive turning with dopamine agonists, a unilateral pallidotomy (ipsilateral to the substantia nigra lesion) alleviated both body axis asymmetry and abnormal turning.[2] The human correlate seems to be the notion that the scoliosis to the right in patients with postencephalitic parkinsonism with clinically more left-side than right-side involvement was corrected after a right pallidotomy.[5]

Further extrapolation to our patients is impossible because animal models or human data that predict the net effect of a unilateral pallidal lesion in a system of bilateral but asymmetrical nigrostriatal dopamine deficiency and chronic exposure to dopaminergic agents on truncal posture are not available. Consequently, we do not know whether the Pisa syndrome in our patients parallels advanced Parkinson's disease or actually represents an unrecognised delayed effect of unilateral pallidotomies in patients with Parkinson's disease.

We would like this letter to serve as an invitation to continue reporting on the follow-up of pallidotomy in patients, including less obvious clinical and easily overlooked features such as a lean to one side.

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Informed patient consent was obtained for the publication of details of the patients.

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CORRECTIONS

K Talbot. Amyotrophic lateral sclerosis, 2nd edn (*J Neurol Neurosurg Psychiatry* 2007;**78**:109). In this book review the acronym TMS was incorrectly expanded to ''traumatic masturbatory syndrome''; it should actually be ''transcranial magnetic stimulation''. In addition, the first sentence should read:

Amyotrophic lateral sclerosis, through its first edition, has become the standard text for clinicians and researchers in the field of ALS/MND.

The online version has been corrected. We sincerely apologise for these errors introduced on copyediting.

A Larner. How to examine the nervous system, 4th edn (*J Neurol Neurosurg Psychiatry* 2007;**78**:110). In this book review the book details were incorrectly published. The correct book review details are:

Edited by R T Ross. Published by Humana Press, New Jersey, 2006, £36.00 (hardback), pp 242. ISBN 1-58829-811-6.

The online version has been corrected. We sincerely apologise for this error introduced on copyediting.